PCT/EP03/8669

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Signed R. Mahoney

Dated 25 June 2003

Patents Form 1/77

Patents Act 1977
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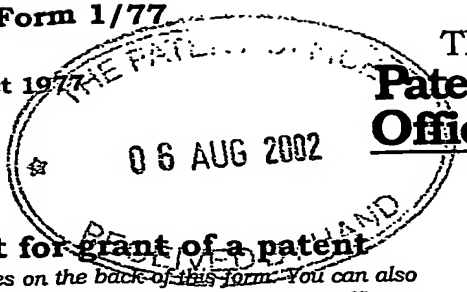

The **Patent Office**

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Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
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1.	Your reference	4-32527P1	
2.	Patent application number *(The Patent Office will fill in this part)*	0218243.4	07AUG02 E739018-1 D00524 P01/7700 0.00-0218243.4
3.	Full name, address and postcode of the or of each applicant *(underline all surnames)*	NOVARTIS AG LICHTSTRASSE 35 4056 BASEL SWITZERLAND	
	Patent ADP number *(if you know it)*		
	If the applicant is a corporate body, give the country/state of its incorporation	SWITZERLAND	7125487005
4.	Title of invention	Organic compounds	
5.	Name of your agent *(If you have one)*		
	"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	B.A. YORKE & CO. CHARTERED PATENT AGENTS COOMB HOUSE, 7 ST. JOHN'S ROAD ISLEWORTH MIDDLESEX TW7 6NH	
	Patents ADP number *(if you know it)*	1800001	

		Country	Priority application number *(if you know it)*	Date of filing (day/month/year)
6.	If you are declaring priority from one ore more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number			

		Number of earlier application	Date of filing (day/month/year)
7.	If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application		

8.	Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:* *a) any applicant named in part 3 is not an inventor, or* *b) there is an inventor who is not named as an applicant, or* *c) any named applicant is a corporate body.* *(see note (d))*	Yes

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9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	3
Claim(s)	1
Abstract	1
Drawing(s)	

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	ONE
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application

Signature Date

B.A. Yorke & Co.

B.A. Yorke & Co. **06 August 2002**

12. Name and daytime telephone number of person to contact in the United Kingdom

Mrs. E. Cheetham
020 8560 5847

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Notes

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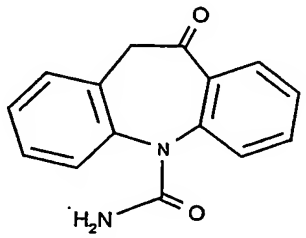
Organic Compounds

The present invention relates to new pharmaceutical uses of a carbamazepine derivative.

More particularly the present invention relates to new pharmaceutical uses for the carbamazepine derivative of formula I



(I)

and their pharmaceutically acceptable salts, hereafter referred to as "the compound".

Oxcarbazepine and the derivative thereof for use in the invention are alternatively know as 10-oxo-10,11-dihydro-5H-dibenz(b,f)azepine-5-carboxamide (Trileptal®).

Oxcarbazepine (10,11-Dihydro-10-oxo-5H-di-benz[b,f]azepine-5-carboxamide) is a known anticonvulsant drug useful in the treatment of seizures of, for example, epileptic origin. Its preparation is described, e.g., in the German patent 2,011,087.

In accordance with the present invention, it has now surprisingly been found that the compound of formula I in free base or acid addition salt is also useful in the prevention and treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

The activity in tinnitus of the compound is indicated in standard tests, e.g. in the salicylate-induced tinnitus model.

It has been demonstrated [C.A. Bauer et al., Hearing Research 147 (2000) 175-182] that chronic salicylate exposure causes upregulation of glutamic acid decarboxylase (GAD) expression in the rat inferior colliculus (IC), associated with the development of tinnitus.

Furthermore, electrophysiological recordings from auditory neurons using patch clamp recording techniques [D. Peruzzi et al. Neuroscience 101 (2000) 403-416, X. Lin et al., Journal of Neurophysiology 79 (1998) 2503-2512] and single neuron recordings [J.J. Eggermont and M. Kenmochi, Hearing Research 117 (1998) 149-160] showed that the excitability of neurons is changed following salicylate and quinine treatment.

Administration of salicylate or quinine caused an increase in the firing rate auditory neurons measured by extracellular electrophysiological recording techniques. Using in vitro electrophysiological recording techniques superfusion with salicylate increases the excitability of the recorded neurons. On administration of the compounds at concentrations of about 1nM to 300 μM, the effects of salicylate were reversed.

For the treatment of tinnitus, appropriate dosage will of course vary depending upon, for example, the compound employed, the host, the mode of administration and the nature and severity of the condition being treated. However, in general, satisfactory results in animals are indicated to be obtained at a daily dosage of from about 1 to about 300 mg/kg animal body weight. In larger mammals, for example humans, an indicated daily dosage is in the range from about 10 to about 3000 mg of a compound according to the invention, conveniently administered, for example, in divided doses up to four times a day.

The compounds may be administered in any usual manner, e.g. orally, for example in the form of tablets or capsules, or parenterally, for example in the form of injection solutions or suspensions.

The present invention also provides pharmaceutical compositions comprising the compounds in association with at last one pharmaceutical carrier or diluent for use in the treatment of tinnitus. Such compositions may be manufactured in conventional manner.

Unit dosage forms may contain for example from about 2.5 mg to about 1000 mg of the compound.

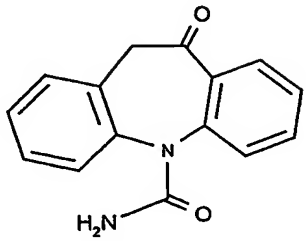
The invention further provides the use of a compound according to the invention for the manufacture of a pharmaceutical composition for the treatment of tinnitus and other inner

ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

The invention further provides a method for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease in a subject in need of such treatment, which comprises administering to said subject a therapeutically effective amount of a compound according to the invention.

CLAIMS

1. The use of a compound of formula I



(I)

and their pharmaceutically acceptable salts, for the treatment of tinnitus.

2. A pharmaceutical composition which incorporates as active agent a compound of formula I according to claim 1 in free or pharmaceutically acceptable salt form, for use in the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

3. The use of a compound of formula I according to claim 1, in free or pharmaceutically acceptable salt form, for the manufacture of a pharmaceutical composition for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease.

4. A method for the treatment of tinnitus and other inner ear/cochlear excitability related diseases such as neuronal loss, hearing loss, sudden deafness, vertigo or Meniere's disease in a subject in need of such treatment, which comprises administering to said subject a therapeutically effective amount of a compound of formula I according to claim 1 in free or pharmaceutically acceptable salt form.

Abstract:

The present invention relates to the use of a carbamazepine derivative in treating tinnitus.